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108 TA(Y	16; TC(S				378 AGA R
ATC			ATG M	CAA Q	GAG
GCC			ACC	AAG K	GCT
99 AAG K	153 TAC Y	207 CGG R	261 CCC P	315 ATC I	369 TCT S
CCC	AAG K	CCT P	GAC	GCC	CAG Q
				GTG	
90 TAC Y	144 TYC F	198 GGC G	252 TCC S	306 CCT P	360 CGT R
AGC					
TCC S	GTA V	GCC	ATG M	GTG V	ACA T
81 TCC S	135 AAG K	189 ATC I	243 GCC A	297 AAA K	351 ACC T
9	CAG Q	TGC	GAC D		
TCC	ATT I	TTC	GAC D	CCG	AAG K
72 GGA G	126 CGC R	180 CTG L	234 ACC T	288 ACT T	342 GAC D
ATG M	GGA G	GAC D	ACC	CGC R	GAG
		ATG M	CTG	GAA E	GTC V
	117 ATC I	171 ATC I	225 CTG L	279 TCA S	333 GGT G
	GAC D	GAC D	TCC	AAT N	GCT
, D	13	ည္ပ	TC	GCG	TCC
	ATG GGA TCC GGC TCC TCC AGC TAC CGG CCC AAG GCC M G S G S S Y R P K A	63 72 81 90 99 CGC AGG TCC TCC AGC TAC CGG CCC AAG GCC ATC M G S G S S Y R P K A I 117 126 136 AG GTA ATC TTC AGG AAG GTA ATC TTC AGG AAG TAC TGC AAC I F S K Y C N	63	State Stat	Hand Hand

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FIGUREIA

432 GCA A	486 CAG Q	540 GCG À	594 GAA E	648 AAA K	702 CTG L	756 AAC N
GGA G	TAC Y	CTG	GCT	CTA L	GAG E	GAT D
GAA E	TGC			GGA G		
423 AGG R	477 GGC G	531 AGC S		639 GAA E		747 TTT F
CGG R	CAG Q	CAG Q	GAA E	TTG L	ATG M	AGT S
<u>CC</u>		ATC I	AAT	GAÄ E		
414 CAG Q	468 GAG E	522 T'TA L	576 ATC I	630 GTG V	684 AAG . K	738 AAG 7 K
GAG E	AGA R	GAA E	AAA K	CGC	ATT I	TGT
CTG	CCC	GAA E	TTC F	AAA K	GAC D	CCC
405 GGC G	459 AGG R	513 AGA R	567 GCA A	621 GAG E	675 AGT S	729 TGC C
	CCC			CTA L	AAG K	AAC N
GTT V	GAG E	CCA	TCA	GTC V	TGC	ACC
396 CGG R	450 GTA V	504 CCT P	558 TTC F	612 GCT A	666 AAA K	720 AGG R
AGA R	CAG Q	ATC I	CAG Q	TYG	GAG E	AGC
GAC D	GGA G	CGC R	GAG E	CAC '	ATT I	AGC S
	441 AGT S	495 CAG Q	549 GCA A	603 AAT N	657 GAG E	711 AGA R
CCA CTG P L	: GAA E	9 9	GTT V	GCA	GTG V	GCC
CCA P	T'T'T F	GAA E	CAG Q	GTT GCA V A	GTG V	GCG A

FIGURE1B

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	810 CTC L	86 TG	918 CTC	972 GTC V	.026 GTC V	080 TCA S	134 CAT H
	CTG	C L	998	'JGT	်ပ္သို့	TC	1 AC
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	801 AAG K	855 GTC V	909 GAC D	963 CTG L	1017 1026 G CAC TGC TTC TGC GTG H C F C V	.071 GAG E	125 GAT D
	CCC	GAC D	CAC H	TGG W	CAC H	1 CAG Q	1 CAC H
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	792 ACT T	84(AC(T	90(ATC M	954 AGC R	1008 TTC F	1062 AGT S	.116 ATC I
	CCC	CCG	CAC H	CTC	AAC	TGC C	GCC A
	GTT V	AAG K	GAG E	ACC	CAC H	CTC L	GCG
	783 GAT D	837 CGG R	891 CTG L	945 GTC V	999 TTC F	053 TGG W	107 ACA T
	CGC R	CTG L	TGC	CCT P	AC CCC TTC CAC AAC TTC CGG CA	1 GTC V	ATG M
	CGA R	C) FL	ra: U)	a	~ ~	7 4	7 · 7
	774 CCT P	828 GAG E	882 CTG L	936 ATC I	990 AAC N	044 AGC S	098 ATC I
	ACT	ATC I	ATG M	AGC S	990 TAC AGA AAC 7 Y R N I	1 TAC Y	1 CTG L
	${ m TTG}$	ACC T	GAG E	TTC	TAC Y	ATG M	ATC I
	765 AAG K	815 GAC E	373 AAT)27 3AC	981 AAC N	1035 ATG M	1089 GAT D
	765 CAC AAG AAG H K K	CCA P	CCC	AGG R	GAC D	1 CAG Q	1 ACG T
	CAC H	TCT	GAG CCC A	GTC V	CAC GAC H D	GCC	CAA ACG Q T

FIGURE 1C

.188 CGC R	242 ATC I	296 AAG K	350 CAT H	404 AAC N	458 rct 3	512 3AG
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GCC	TTC	999 9	GCA	TAC	GAT D	TTA L
1179 CTG L	1233 GCC A	1287 GAT D	.341 ATG M	.395 GAC D	449 TGT C	503 TGT C
GAG	GTG V	CCT P	J GAC D	1 TYT F	TGC C	1 3AC D
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1170 CGC R	1224 TGC C	1278 ATC I	1332 GCC A	1386 GAG E	.440 ATA I	494 TGG W
GCC	CAC H	AAC	TTG L	J ATG M	1 TTG L	1 CCT P
AAT N	CAC H	TCC	ATC	AAA K	ATT I	GAG
161 ATC I	215 AAC N	269 I'TC F	323 FTA L	377 3AG	131 ATG	185 3CA (
1 G	1 [G]	C T	1 4 1	1; A (14 G 2	14 C C
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TAC Y	CTG	AAC N	ATC I	TTC	CTG L	GAA E
.152 ACG T	206 CCG P	260 TGC C	314 ATG M	368 TCT S	422 CTG L	476 ATG M
AAC N	ICA S	3AG	3GA	1 SAT	ACC .	CA C
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1143 TAC Y	1197 1206 1215 1224 1233 1242 GAC ATC TCA CCG CTG GAG AAC CAC TGC GCC GTG GCC TTC CAG ATC D I S P L E N H H C A V A F Q I	1251 GAG E	1305 CGA R	.359 ATT I	1413 CAC H	1467 GTC V
ر 967 9	1 AAT N	GCC A	ATC I	1 GAA E	1413 GAG CAC E H	1 GAG E
1143 CCC GGC TAC P G Y	1197 TAC AAT GAC Y N D	1251 CTC GCC GAG L A E	1305 CAG ATC CGA (Q I R (1359 GCA GAA ATT A A E I N	GAG E	1467 AAC GAG GTC N E V

FIGUREID

-	1557 1566 C CTT CCT GTG GCA CCG L P V A P	1611 1620 G ATT GGG TTC ATC AAG I G F I K	1665 1674 C TTC CCC ATG GTT GAG F P M V E	1719 1728 C TAC GAG GAG CTG AAG Y E E L K	GAT GAC GCC ATG AAA GAG TTA CAG AAG AAG ACT GAC AGC TTG ACG TCT D D A M K E L Q K K T D S L T S	1827 1836 3 AAA AAC AGT GAA GGA K N S E G	1881 1GG ACG GGC TGG CCG
	9 9	CA O	ŗ 1	о В	AC	GT/C	
	1548 TCA GAA S E	1602 ACA GCC T A	1656 ACC AAG T K	1710 CGA GAT R D	1764 AAG AAG K K	1818 AGA GAT R D	1872 CTG CAG
	AAG K	GCC	GTG V	TCC	CAG Q	AGC S	TGG
	1539 CGT GAG R E	1593 ACC AAG T K	1647 GAA ACA E T	1701 TGG GAA W E	1755 GAG TTA E L	1809 3AG AGA . E R	1863 3GG GCG
	GAC D	GTG V	TYTT	CTT	AAA K	AGA (990
	1530 2AG AGC 2 S	1584 iac aaa) K	1638 CA ATG	1692 AG CCA	1746 CC ATG	1800 AG TCC S	1854 GA AAG
	ATG (CGA G	ATC C	CTG C	GAC G	GAG A E K	TGA G
	1521 GAA TAT TTT E Y F	1575 TTC ATG GAC F M D	1629 GTC CTG V L	1683 GAG ATC ATG E I M	1737 ATA GAT I D	1791 GGG GCC ACC G A T	1845 1854 1863 GAC TGT GCC TGA GGA AAG CGG GGG GCG D C A
	GAA E	TTC	TTT	GAG	CGG	999	GAC '

FIGURE 1E

FIGURE 1F

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1935 A CCT	•) •	1989	DDD
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1926 A GAG CTG CCC TGG			ACA
1926 3G CCC) 	1980	GAT
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GAG			THU
1917 3G GAA		1971	TTG
1917 AGG GAA			ATT
TGC			ACC
1908 A TCC TTG		1962	AGA
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FIGURE 2A

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FIGURE 2B

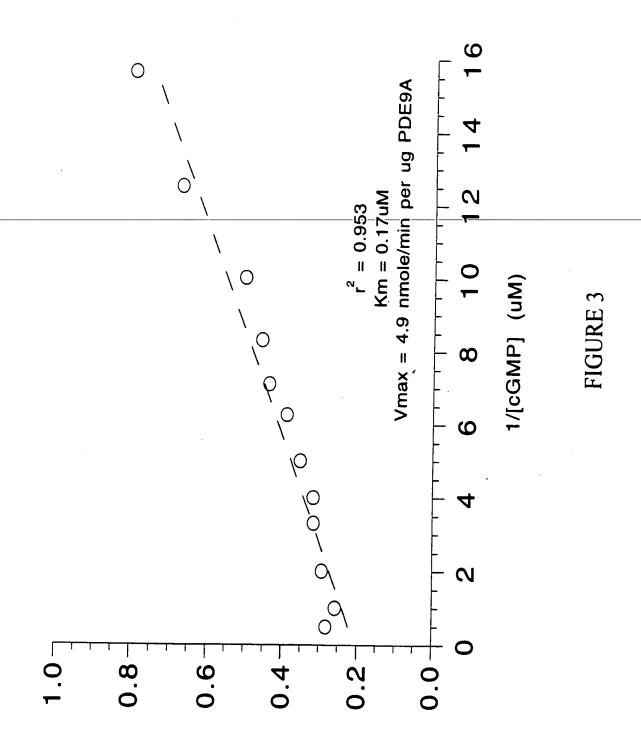
g829179 q829179 g829179 g829179 PDE9A PDE9A PDE8A PDE9A PDE9A PDE8A PDE9A PDE8A PDE8A PDE8A FDM F. TEMTK P LIA S LFA TELAVRYNDISPLENHHCAV SELAILYNDTAVLESHHAAL SELALMYNDESVLENHHLAV <u>日</u> P E ANYHS E LM H Z HDNY Ø Ø 24 V A MVLAT G 口 EVINTMI GSGVLLI G EPE-CNIFSNIPPDGFKQIRQGMITLILA GDDKCNIFKNMERNDYRTLRQGIIDMVLA NQG-CDIFCNMQKKQRQTLRKMVIDIVLS DFSINPVTLRRWLFCVH FLHCSESTLRSWLQIIE SLMIPPKTFLNFMSTLE E N Н ഠ I Ω Ц Д Д a CSLOEKFSC KERIKETLDF PALEGVETF LOEKF OA TDKNTKKV 1 म ſΉ Ŀ Γ CE N G SN LSK SMVW DY L C N A G 24 ſΞ STHSADVLHATAYF SLHAADVTOSTNVL ם ם OINA Ы Z \vdash Ω 田田 LVR CVAOMMY L A L A 回 ARFGICI KM 8 0 0 Fi Ei Ei Y L Д INK 回 G K T N N C L T I N N N X Q 1 田 S Z TH TH RHCF AICHDLDHPG ATIHDVDHPG HMY ı PLIYLGLKM PLTCVAYTI Ы 된 V ı 田 [L <u>[</u>] S EHVNK HDV 田 E O Ω ĪΨ A N P F H N N P Y H N N P Y H N N O I L K L L Z Ι H S 면 된 ഥ' വ Ö 压 H A[Z A 272 397 204 309 437 244 349 517 389 557

FIGURE 2C

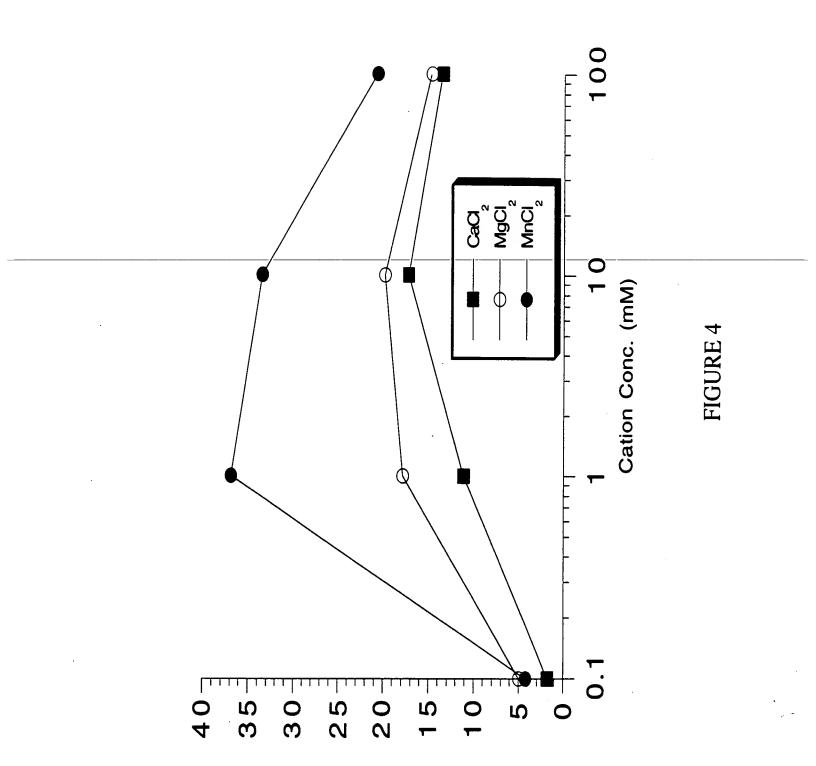
449 HMTLLKMILIKCCDISNEVRPMEVAEPWVDCLLEEYFMQS 597 NRTLIKRMLIKCADVSNPCRPLQYCIEWAARISEEYFSQT 392 DRIQVLENLVHCADLSNPTKPLPLYKRWVALLMEEFFLQG		PDE9A PDE8A g829179
489 DREKSEGLPVA - PFMDRDKVTKATAQIGFIKFVLIPMFET 637 DEEKQQGLPVVMPVFDRNTCSIPKSQISFIDYFITDMFDA 432 DKERESGMDIS - PMCDRHNATIEKSQVGFIDYIVHPLWET		PDE9A PDE8A g829179
528 VTKLFPMVEEIMLOPLW 677 WDAFV DLPDLMOHLDNNFKYWKGL 471 WASLVHPDAQDILDTLEENRDYYQSMIPPSPP		PDE9A PDE8A g829179
545 - ESRDRYE - ELKRIDDA - MKELOKKTDSL 701 DEMKLRNLRPPPE 511 QEDRIRFQVTLEESDQENLAELEEGDESGGET	TSGA PE PE TTTTGTTGT 98	PDE9A PDE8A g829179
575 TEKSRERSRD VKNSEGDCA 713 551 TAASALRAGGGGGGGGMAPRTGGCQNQPQHG	₩ S	PDE9A PDE8A g829179

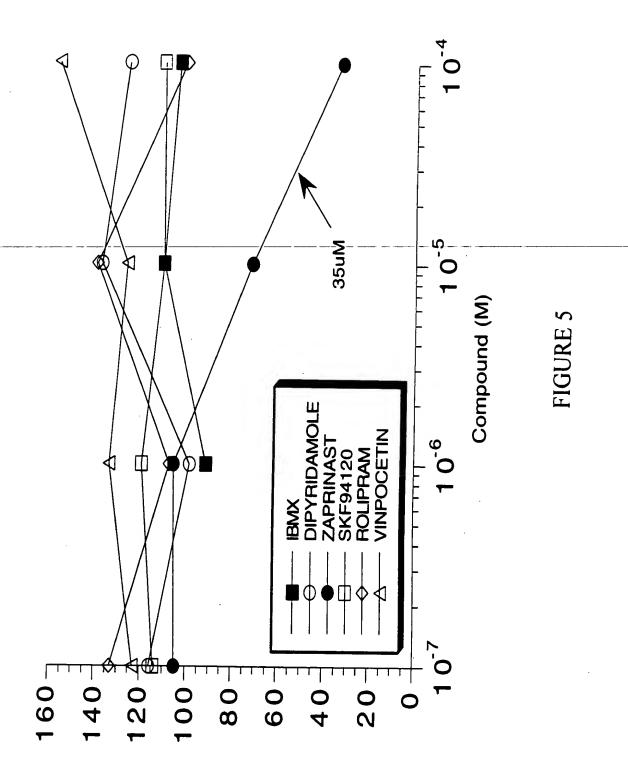
FIGURE 2D

1/V (nmoles/min per ug PDE9A)



cGMP Hydrolysis (% conversion)





cGMP Hydrolysis (% control)